# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**REQUEST FOR FILING**
**(RULE 53(b)(1))**

For Design or Utility Applications

Rule 53(b)(1) PATENT APPLICATION: **(DO NOT USE FOR CIPs)**

☐ Continuation )
☐ Divisional ) application under 37 CFR 1.53(b)(1)
☐ Substitution under 37 CFR 1.53(b)(1)
☐ Reissue of pending prior application of

Group Art Unit: 1641

Examiner: Baskar

Inventor(s): PENFOLD ET AL

Appl. No.: 08 (Series Code ⇧) | 935,537 (Serial No. ⇧)

Atty. Dkt. PM 266810 (New M#) | R.3250 (Client Ref)

Filed: September 23, 1997

Title: ASSAY REAGENTS AND DEVICES

Date: April 25, 2000

Asst. Commissioner of Patents and Trademarks
Washington, DC 20231

(Parent Matter No. 241997 )

Sir:

To effect the above-requested filing today:

1. **Attached** is a copy **(which must be filed)** of the prior application, including:

- ☒ Abstract
- ☒ Specification and claims (10 pages) **(must be attached)**
- ☐ Drawings **(must be attached if originally filed):** _____ sheet(s)/set: ☐ 1 set informal; ☐ Formal of size ☐ A4 ☐ 11"

1A. Always X one box, only:
(1) ☒ Signed declaration or oath as originally filed in prior application attached
(2) ☐ NO declaration or fee is enclosed; therefore, this is a filing under Rule 53(f).

2. ☐ This application is hereby filed by less than all of the inventors named in the prior application. Petition is hereby made requesting deletion as inventor(s) of the following who is/are **not** inventor(s) of the invention being claimed in this application:

1. _____ 2. _____
3. _____ 4. _____
5. _____ 6. _____
7. _____ 8. _____
9. _____ 10. _____

3. The entire disclosure of the prior application is considered as being part of the disclosure of the accompanying application and is hereby incorporated therein by reference thereto.

4. ☒ Priority is claimed under 35 U.S.C. 119/365 based on filing in Europe (country) of

| | Application No. | Filing Date | | Application No. | Filing Date |
|---|---|---|---|---|---|
| (1) | 96307078.4 | Sept. 27, 1996 | (4) | | |
| (2) | | | (5) | | |
| (3) | | | (6) | | |

a. ☐ _____ (No.) Certified copy/copies attached.
b. ☒ Certified copy/copies previously filed on September 23, 1997 in U.S. Application No. 08/935,537 , filed on September 23, 1997.
series code ⇧ ⇧ serial no.
c. ☐ Certified copy/copies filed during International stage of PCT/ _____/_____ .

4. (a) ☐ Domestic priority is claimed from PCT/ _____/_____ , filed _____ .
(b) ☐ Benefit is claimed of Provisional Application No. 06/_____ , filed _____ .

5. ☒ Prior application is assigned to Unilever Patent Holdings BV

by assignment recorded April 3, 1998 (Date) Reel 9085 Frame 0645.

6. ☒ Attached is the following number of Assignments (including original and all later successive ones by different assignors): 1 and respective **new** Cover Sheets. (Do **NOT** file old cover sheets.)

(Assignments in parent **must be refiled** with new Cover Sheets in this continuing application if you want it/them recorded against the continuing application.)

Please return the recorded Assignment to the undersigned.

7. ☒ The power of attorney in the prior application is to Paul N. Kokulis (Reg. No. 13023) of Pillsbury Madison & Sutro LLP
(Name and Reg. No.)
whose current address is as in item 8 below.

a. ☐ Recognize as associate attorney _____
(Name, Reg. No. and Address)

8. **Address all future communications to Intellectual Property Group of Pillsbury Madison & Sutro LLP, Ninth Floor, East Tower 1100 New York Avenue, N.W., Washington, D.C. 20005-3918**

9. ☒ **Amend the specification** by inserting before the first line the sentence:--This is a ☐ continuation ☒ division of Application No. 08/935,537, filed September 23, 1997
series code ⇧ ⇧ serial no.
.--

9. (a) ☐ **Amend the specification** by inserting before the first line: --This application claims the benefit of Provisional Application No. 60/_____, filed _____ .--

10. ☐ It has been recently determined that this new continuing application is entitled to small entity status. Hence:
___ (No.) Verified Statement(s) establishing "small entity" status under Rules 9 & 27 were/are:
☐ filed in above prior application (and hence applicable hereto)
☐ attached.

11. Petition to extend the life of the above prior application to at least the date hereof
(one box) ☐ is being concurrently filed in that prior application (Use Form PAT-111).
(must be) ☐ was previously filed in that prior application (Check length of prior extension).
(X'd) ☒ is not necessary for copendency (**Double check** before X'ing this box).

12. ☒ **INFORMATION DISCLOSURE STATEMENT:** Attached is Form PTO-1449 listing all of the documents cited by Applicant and the PTO in the parent application(s) relied upon under 35 USC 120 and referenced in item 9 above. Per Rule 98(d) copies of those documents are not required now. Please consider those documents and advise that they have been considered in this new application as by returning a copy of the enclosed Form PTO-1449 with the Examiner's initials in the left column per MPEP 609. .

13. ☐ Attached is a Rule 103(a) Petition to Suspend Action.

14. ☐ **PRELIMINARY AMENDMENT to be entered before fee calculation:** (Do not make amendments here except for correction of improper multiple dependencies or cancellation of whole claims or multiple dependencies for purpose of reducing the filing fee per MPEP §§ 506 and 607; do not cancel all claims).

**FILING FEE**

THE FOLLOWING FILING FEE IS BASED ON

->->->->CLAIMS AS FILED AND **CHANGED BY PRELIMINARY AMENDMENT IN ITEM 14**<-<-<-<-

NOTE: If box 1A2 is X'd, do not pay fees, but leave lines 15-22 and 27-32 blank.

| | | | | Large/Small Entity | | Fee Code |
|---|---|---|---|---|---|---|
| 15. Basic Filing Fee . . . . . Design Application | | | | $310/$155 | | 106/26 |
| 16. Basic Filing Fee . . . . . Not Design Application | | | | $690/$345 | +690 | 101/201 |
| 17. Total Effective Claims | 11 | minus 20 = | 0 | x $18/$9 | +0 | 103/203 |
| 18. Independent Claims | 1 | minus 3 = | 0 | x $78/$39 | +0 | 102/202 |
| 19. If any proper multiple dependent claim (ignore improper) is present, | | | | $260/$130 | +0 | 104/204 |
| 20. | | | | **Subtotal =** | **$690** | |
| 21. If "petition" box 13 above is X'd, add petition fee. . . . . $130 | | | | | +0 | 122 |
| 21A. If box 6 above is X'd, add Assignment recording fee . . . . . $ 40 | | | | | +40 | 581 |

22. **TOTAL FILING FEE ATTACHED =** **$730**

(carry forward to Item 31)

23. ☐ ATTACHED:

24. ☒ Preliminary Amendment attached (to be entered after assigning Appln. No.)

25. ☐ The following PRELIMINARY AMENDMENT is to be entered after assigning Appln. No.:

26. **ADDITIONAL FEE CALCULATION FOR PRELIMINARY AMENDMENT PER BOXES 24/25**

| | Claims remaining after amendment | Highest number previously paid for | Present Extra | | | | Additional Fee | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Large/Small Entity | | | File Code |
| 27. Total Effective Claims | *11 | minus ** 20 | = 0 | x | $18/$9 | = | $ 0 | (103/203) |
| 28. Independent Claims | *1 | minus *** 3 | = 0 | x | $78/$39 | = | + 0 | (102/202) |
| 29. If amendment enters proper multiple dependent claim(s) into this application for the first time, add (per application) ..... | | | | | $260/$130 | | + 260 | (104/204) |
| 30. | | | | | ADDITIONAL FEE | | $ 260 | |
| 31. | | | | | plus **FEE** from item 22 on page 3 | | + | |
| 32. | | | | | **TOTAL FEE ATTACHED** | | $ 990 | |

33. *If the entry in this space is less than a entry in the next space, the "Present Extra" result is "0"

34. **If the "Highest number previously paid for" (see item 17 above) is less than 20, write "20" in this space

35. If the "Highest number previously paid for" (see item 18 above) is less than 3, write "3" in this space

Our Deposit Account No. 03-3975
Our Order No. 60113 (C#) | 266810 (M#)

**CHARGE STATEMENT:** Upon the filing of a Declaration pursuant to Rule 60(b) or 60(d), the Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown above for which purpose a duplicate copy of this sheet is attached.
**This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.**

**Pillsbury Madison & Sutro LLP**
**Intellectual Property Group**

1100 New York Avenue, NW
Ninth Floor
Washington, DC 20005-3918
Tel: (202) 861-3000
PNK/MAH
Atty./Sec.

**By Atty:** Paul N. Kokulis **Reg. No.** 16773
**Sig:**
**Fax:** (202) 822-0944
**Tel:** (202) 861-3503

**NOTE No. 1:** File this Request in duplicate with 2 postcard receipts (PAT-103) & attachments
**NOTE No. 2:** Is extension in parent necessary for copendency? **DOUBLE CHECK** Item 11 above.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

PENFOLD ET AL

Serial No.: Division of 08/935,537 Group Art Unit: 1641

Filed: April 25, 2000 Examiner: Baskar

Title: ASSAY REAGENTS AND DEVICES

April 25, 2000

PRELIMINARY AMENDMENT

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Please amend the above divisional application as follows:

IN THE SPECIFICATION

Page 1, line 11, after "EP-A-291194", insert -- (equivalent to U.S. 5,622,871) --;

line 19, correct the spelling of "reassure"; and

line 27, change "feint" to -- faint --.

Page 6, line 22, change "feint" to -- faint --.

IN THE CLAIMS

Cancel claim 1 without prejudice.

Claim 2, line 1, change "A reagent" to -- An assay device --; and change "1" to -- 9 --.

Claims 3 and 4, line 1 of each, change "A reagent" to -- An assay device --.

Claim 5, line 1, change "A reagent" to -- An assay device --; and change "1" to -- 9 --.

Claims 6 and 7, line 1 of each, change "A reagent" to -- An assay device --.

Amend claim 9 as follows:

9. (Amended) An assay device of the type wherein a sample liquid reconstitutes a labelled reagent and carries it into a detection zone and a control zone, binding of said labelled reagent in these zones revealing the assay result, wherein said labelled reagent [is as claimed in claim 1] comprises a particulate direct label co-sensitized with

(i) a specific binding agent having specificity for an analyte or analyte analogue, and

(ii) a non-specific protein which can participate in a control reaction with another specific binding agent which does not bind to said first specific binding agent nor participate in the formation of a complex by means of which detection of said analyte or analyte analogue is accomplished in said detection zone.

Claim 10, last line, change "first particles" to -- particulate direct label --.

Claim 11, line 1, after "9", insert -- or claim 10 --.

## REMARKS

The present divisional application includes claims 2-11 and is directed towards subject matter which was non-elected in the applicants' parent case, i.e. claims 8-11.

Claims 2-7 have been appropriately amended to depend, directly or indirectly, from claim 9.

Attached is a PTO-1449 listing the art of record in the applicants' parent case.

Favorable action is requested.

Respectfully submitted,

PILLSBURY MADISON & SUTRO LLP

By _____
Paul N. Kokulis
Reg. No. 16773

PNK:mh
1100 New York Avenue, N.W.
9th Floor – East Tower
Washington, D.C. 20005-3918
Phone: (202) 861-3503

# APPLICATION UNDER UNITED STATES PATENT LAWS

Invention: ASSAY REAGENTS AND DEVICES

Inventor (s): Yvonne E. JOBLING
David A. PERCIVAL

Cushman Darby & Cushman
Intellectual Property Group of
Pillsbury Madison & Sutro LLP
1100 New York Avenue, N.W.
Ninth Floor, East Tower
Washington, D.C. 20005-3918
Attorneys
Telephone: (202) 861-3000

This is a:

- ☐ Provisional Application
- ☒ Regular Utility Application
- ☐ Continuing Application
- ☐ PCT National Phase Application
- ☐ Design Application
- ☐ Reissue Application
- ☐ Plant Application
- ☐ Substitute Specification
  Filed _____
  in App. No. ___/_____

## SPECIFICATION

# ASSAY REAGENTS AND DEVICES

## FIELD OF THE INVENTION

This invention relates to reagents useful in immunoassays and to assay devices using such reagents.

## BACKGROUND TO THE INVENTION

Many assays are now available which utilise the technology described in EP-A-291194, wherein a particulate direct label such as a gold sol or coloured latex particle is used to reveal the result of an assay conducted in a porous carrier such as a porous strip. Concentration of the particulate label in a comparatively small detection zone in the strip reveals the assay result. It is common practice for the strip to include a control zone, normally located downstream from the detection zone, in which a coloured signal is also generated to reasure the user that the test has been correctly performed. In most commercial products based on this concept, the test and control signals are generated using the same particulate label.

This technology copes very well with most assay situations, but there can be extreme situations in which the clarity of the signals could be improved For example, the control zone signal may appear rather feint if the concentration of analyte is very high and is causing most of the particle label to become bound in the detection zone, leaving insufficient label to carry through and provide a strong control signal.

An objective of the present invention is to provide reagents and assay devices in which improved clarity of assay signals are obtained irrespective of the amount of analyte that may be present in a sample being tested.

A further objective is to provide good clear assay signals without the use of excessive amounts of labelled reagent.

**GENERAL DESCRIPTION OF THE INVENTION**

By the invention we provide a reagent useful in immunoassays, comprising a direct particulate label co-sensitised with a specific binding agent having specificity for an analyte or analyte analogue and with a non-specific protein which can participate in a control reaction with another specific binding agent which does not bind to the first specific binding agent nor participate in the formation of a complex by means of which detection of the analyte or analyte analogue is accomplished.

Preferably the quantity of specific binding agent on the co-sensitised particle exceeds the quantity of non-specific protein thereon. Preferably there is at least a 2:1 ratio by weight between these two materials on the particle. More preferably at least about 5:1, ideally about 10:1. The primary specific activity, in terms of analyte-binding and control signal formation, is therefore heavily biassed in favour of analyte-binding.

Optionally, the reagent additionally comprises a second population of the direct particulate label sensitised solely with the non-specific protein.

Preferably the first specific binding agent is an antibody raised in a first species and the non-specific protein is an immunoglobulin from another species. For example, the first specific binding agent can be a murine antibody.

The non-specific protein can be a rabbit immunoglobulin, for example, but any immunoglobulin from any species can be used provided that it does not bind either to the analyte or to any reagent that participates in detection of the

analyte.

A preferred reagent according to the invention comprises coloured latex particles of diameter less than 0.5 micron, co-sensitised with an anti-hCG murine monoclonal antibody and with rabbit IgG. Preferably this reagent additionally comprises same-coloured latex particles of diameter less than 0.5 micron sensitised solely with rabbit IgG, the weight ratio of the co-sensitised particles to the second particles being at least 2:1, more preferably about 3:1.

Another embodiment of the invention is an assay device of the type wherein a sample liquid reconstitutes a labelled reagent and carries it into a detection zone and a control zone, binding of the labelled reagent in these zones revealing the assay result, characterised in that the labelled reagent is as described in any one of the foregoing paragraphs.

Preferably the detection zone contains an immobilised specific binding agent which acts as a direct or indirect capture means for the analyte or analyte analogue but which does not bind to the non-specific protein, and the control zone contains a specific binding agent which binds the non-specific protein but does not bind the specific binding agent co-sensitised on the first particle.

The particles can be any micro-particles that can be used as mobile labels in strip-format assays. Such assays are described in many publications, including EP-A-291194, EP-A-383619, WO 96/09553 and WO 96/09546. Appropriate particles include latex (polystyrene) particles, usually of diameter less than about 0.5 micron, metal sols, such as gold sols, non-metallic elemental sols, such as selenium or carbon, and dye sols.

The invention will be described with particular reference

to test kits useful in monitoring of body fluid analytes, and especially to home monitoring of urinary analytes of relevance to the determination of pregnancy (hCG) or of the fertility status of the human ovulation cycle (by measuring LH and/or E3G and/or P3G, for example). This is by way of example only, and it will be appreciated that the invention is useful in many other contexts where other sample liquids and analytes are involved, such as assays for cancer markers, cardiac markers, blood glucose, drugs of abuse, hormones, infectious disease markers, tests in therapeutic drug monitoring, manufacturing and raw material quality control, and tests for effluent and pollution levels.

Preferably the detection zone contains an immobilised specific binding agent which acts as a direct or indirect capture means for hCG, the control zone contains an immobilised anti-rabbit IgG antibody, and the mobile labelled reagent comprises coloured latex particles of diameter less than 0.5 micron, co-sensitised with an anti-hCG murine monoclonal antibody and with rabbit IgG.

Preparation of the novel reagents of the invention, and the manufacture of assay devices using these novel reagents, can both be accomplished using conventional procedures. The co-sensitised particulate label can be prepared by contacting commercially-available particulate labels, such as latex (polystyrene) particles of appropriate dimension, in aqueous suspension with a mixture of the two materials with which the particles must be sensitised. For example, these materials can be a mixture of a murine monoclonal antibody directed against the alpha-chain of hCG, together with a non-specific polyclonal antibody such as rabbit IgG. These materials need to be present in an appropriate weight ratio, as described elsewhere herein. The co-sensitisation needs to be conducted under buffered conditions, as is standard practice. Following a sufficient time interval to allow the materials to deposit onto the particles, unbound

materials can be separated by conventional procedures such as centrifugation, filtration and/or ultra-filtration and the co-sensitised particles resuspended in a conventional storage buffer solution ready for use in the preparation of an assay. A specific example of a co-sensitisation procedure is given below.

In order to describe the benefits of the invention in more detail, we can consider as an example its applicability in the context of a pregnancy test based on the immunochromatographic format using coloured latex particles as a mobile direct label in an assay strip. The assay strip, which is, for example, made from nitrocellulose of pore size about 8 microns backed with "Mylar" polyester, includes two transverse lines of deposited immobilised specific binding reagents, namely a test line containing an anti-β hCG murine monoclonal and a control line downstream from the test line containing an immobilised murine monoclonal raised against rabbit IgG. At a location upstream from the test line is a mobile reagent comprising coloured latex particles of diameter approximately 0.3 microns. This location can be on the nitrocellulose or in a separate pad or wick of porous material which is upstream in the flow path by which sample liquid (urine) can reach the nitrocellulose. The mobile reagent comprises two populations of latex particles, namely:

a) particles co-sensitised with an anti-α hCG murine monoclonal and with the same rabbit IgG against which the control line antibody was raised; and

b) a second population of the same latex particles simply bearing the rabbit IgG.

Application of a urine sample will mobilise the latex particles. If the urine contains hCG, a sandwich complex can form between the anti-hCG monoclonal on the co-

sensitised particle and the anti-hCG antibody in the test line. In consequence, at least some of the co-sensitised particles will become bound in the test line to provide a coloured signal indicative of the presence of hCG. Remaining mobilised co-sensitised particles which do not become bound in the test line, eg. because they are in excess relative to the amount of hCG present in the sample, can become bound downstream in the control line by interaction between the control line antibody and the rabbit IgG on the co-sensitised particles. In addition, the second population of latex particles bearing only the rabbit IgG will be mobilised and carried past the test line to reinforce the control signal.

We have found in practice that if the hCG concentration in the urine sample is comparatively high (although not so high as to induce the well-known "hook effect" which causes a drop in the apparent hCG signal) most of the anti-hCG particles are bound in the test line. Typically this will occur if the hCG concentration lies between about 5000 and about 15000 mIU/ml. Under these circumstances there would be a strong test line signal but a rather feint or completely absent control line signal. However, the provision of the second population of latex particles, which cannot possibly bind in the test line, ensures that a strong control line signal is still obtained even under these circumstances. An appropriate blend of the co-sensitised particles and the mono-sensitised particles is about 3:1. In a sandwich-format assay this combination of particles provides a good clear test signal and control signal under most assay conditions, with the exception of extremely high analyte concentrations, while requiring the minimum total number of particles. Substantially more particles would be required if the test signal and control signal were generated by completely separate populations.

**EXAMPLE**

This example describes a sensitisation procedure which can be used to prepare reagents in accordance with the invention.

A latex particle reagent co-sensitised with a murine anti-α hCG monoclonal antibody and with rabbit immunoglobulin can be prepared as follows.

10ml of a commercially available suspension (10% solids) of blue coloured latex particles of diameter about 0.3 microns is added to 40ml of 100mM borate buffer pH 8.5 and stirred vigorously. This mixture is centrifuged for 10 minutes at 13500 rpm and the supernatant liquid removed. The latex pellet is re-suspended in 20ml of the same buffer.

To a separate 20ml of the same buffer are added 400μg/ml of a murine anti-β hCG monoclonal antibody and 50μg/ml rabbit IgG. The latex-containing buffer and the antibody-containing buffer are both heated in a water bath to 40°C and, on reaching this temperature, 5ml of ethanol is added to each. The antibody solution is then immediately added to the latex suspension, mixed using a magnetic stirrer, and incubated in the water bath for 60 minutes. At this point 50ml of a solution of bovine serum albumin (BSA) in the same buffer pre-warmed to 40°C is added and the incubation continued at 40°C for a further 30 minutes. Thereafter the solution is centrifuged for 25 minutes at 13500 rpm and the supernatant removed. The pellet is resuspended in 50ml of 100mM Tris buffer pH 9.0 to provide a suspension containing 2% solids. Optionally preservatives such as sucrose at 20% (w/v) and BSA at 10% (w/v) can be added. This latex suspension is ready for use in the preparation of an assay device.

An identical procedure can be used to prepare latex

particles sensitised solely with the rabbit immunoglobulin. In this instance the 20ml suspension of latex particles is combined with 20ml buffer containing 150μg/ml rabbit IgG.

In the subsequent preparation of an assay device using a combination of the co-sensitised and mono-sensitised particles, the two suspensions of sensitised particles can be combined in appropriate proportions (to provide an appropriate blend, e.g. 3 to 1 of the two populations of particles) and applied as a single combined reagent on a test strip or in a separate pad or wick forming part of an assay device.

**CLAIMS**

1. A reagent useful in immunoassays, comprising a direct particulate label co-sensitised with

(i) a specific binding agent having specificity for an analyte or analyte analogue, and

(ii) a non-specific protein which can participate in a control reaction with another specific binding agent which does not bind to said first specific binding agent nor participate in the formation of a complex by means of which detection of said analyte or analyte analogue is accomplished.

2. A reagent according to claim 1, wherein said first specific binding agent is an antibody raised in a first species and said non-specific protein is an immunoglobulin from another species.

3. A reagent according to claim 2, wherein said first specific binding agent is a murine antibody.

4. A reagent according to claim 2, wherein said non-specific protein is a rabbit immunoglobulin.

5. A reagent according to claim 1, additionally comprising a second population of said direct particulate label sensitised solely with said non-specific protein.

6. A reagent according to claim 2, comprising coloured latex particles of diameter less than 0.5 micron, co-sensitised with an anti-hCG murine monoclonal antibody and with rabbit IgG.

7. A reagent according to claim 6, additionally comprising same-coloured latex particles of diameter less

than 0.5 micron sensitised solely with rabbit IgG, the ratio of said co-sensitised particles to said second particles being at least 2:1.

8. An assay device according to claim 7, wherein said ratio is about 3:1.

9. An assay device of the type wherein a sample liquid reconstitutes a labelled reagent and carries it into a detection zone and a control zone, binding of said labelled reagent in these zones revealing the assay result, wherein said labelled reagent is as claimed in claim 1.

10. An assay device according to claim 9, wherein said detection zone contains an immobilised specific binding agent which acts as a direct or indirect capture means for said analyte or analyte analogue but which does not bind to said non-specific protein, and said control zone contains a specific binding agent which binds said non-specific protein but does not bind said specific binding agent co-sensitised on said first particle.

11. An assay device according to claim 9, wherein said detection zone contains an immobilised specific binding agent which acts as a direct or indirect capture means for hCG, said control zone contains an immobilised anti-rabbit IgG antibody, and said labelled reagent is coloured latex particles of diameter less than 0.5 micron, co-sensitised with an anti-hCG murine monoclonal antibody and with rabbit IgG.

**ABSTRACT**

A reagent useful in immunoassays, comprising a direct particulate level co-sensitised with a specific binding agent having specificity for an analyte or analyte analogue and with a non-specific protein which can participate in a control reaction with another specific binding agent which does not bind to the first specific binding agent nor participate in the formation of a complex by means of which detection of the analyte or analyte analogue is accomplished. Preferably the first specific binding agent is an antibody raised in a first species and the non-specific protein is an immunoglobulin from another species. Optionally, the reagent additionally comprises a second population of the direct particulate label sensitised solely with the non-specific protein.

FOR UTILITY/DESIGN
CIP/PCT NATIONAL/PLANT
ORIGINAL/SUBSTITUTE/SUPPLEMENTAL
DECLARATIONS

**RULE 63 (37 C.F.R. 1.63)**
**DECLARATION AND POWER OF ATTORNEY**
**FOR PATENT APPLICATION**
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**CUSHMAN FORM**

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the INVENTION ENTITLED: ASSAY REAGENTS AND DEVICES

the specification of which (CHECK applicable BOX(ES)

-> [ ] is attached hereto

X -> [X] was filed on 23 SEPT 97 as U.S. Application No. NOT YET KNOWN

Box(es) -> [ ] was filed as PCT International Application No. PCT/ on

-> -> and (if applicable to U.S. or PCT application) was amended on

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 25 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing date of this application:

| PRIOR FOREIGN APPLICATION(S) Number | Country | Day/MONTH/Year Filed | Date First Laid - open or Published | Date Patented or granted | Priority Claimed Yes | No |
|---|---|---|---|---|---|---|
| 96307078.4 | EUROPE | 27 SEPTEMBER 96 | | | YES | |

I hereby claim domestic priority benefit under 35 U.S.C. 120/365 of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

| PRIOR U.S. PROVISIONAL, NONPROVISIONAL AND/OR PCT APPLICATION(S) Application Number (series code/serial no.) | Day/MONTH/Year Filed | Status pending, abandoned, patented | Priority Claimed Yes | No |
|---|---|---|---|---|

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

And I hereby appoint Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro L.L.P. 1100 New York Avenue. N.W., Ninth Floor, East Tower, Washington D.C.20005-3918, telephone number (202) 861-3000 (to whom all communications are to be directed), and the below-named persons (of the same address) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete names/numbers below of persons no longer with their firm and to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/organization who/which first sends/sent/this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct the above Firm and/or a below attorney in writing to the contrary.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Paul N. Kokulis | 16773 | David W. Brinkman | 20817 | Chris Comuntzis | 31097 | James D. Berquist | 34776 |
| Raymond F. Lippitt | 17519 | George M. Sirilla | 18221 | Paul E. White Jr. | 32011 | Timothy J. Klima | 34852 |
| G. Lloyd Knight | 17698 | Donald J. Bird | 25323 | Michelle N. Lester | 32331 | John P. Moran | 30906 |
| Carl G. Love | 18781 | W. Warren Taltavull | 25647 | Jeffrey A. Simenauer | 31993 | Stephen C. Glazier | 31361 |
| Edgar H. Martin | 20534 | Peter W. Gowdey | 25872 | G. Paul Edgell | 24238 | Paul F. McQuade | 31542 |
| William K. West, Jr. | 22057 | Dale S. Lazar | 28872 | Lynn E. Eccleston | 35861 | Barry L. Grossman | 30844 |
| Kevin E. Joyce | 20508 | Glenn J. Perry | 28458 | David A. Jakopin | 32995 | | |
| Edward M. Prince | 22429 | Kendrew H. Colton | 30368 | Mark G. Paulson | 30793 | | |

1) INVENTOR'S SIGNATURE: _____ Date 21/12/97

Inventor's Name (typed) Wynne (First) E. (Middle Initial) PENFOLD (Family Name) United Kingdom (Country of Citizenship)

Residence (City) Bedford (State/Foreign Country) United Kingdom

Post Office Address (Include Zip Code) 3 Clover Avenue, River Meadows, Bedford, MK41 0ST, United Kingdom

2) INVENTOR'S SIGNATURE: _____ Date 22nd Dec 1997

Inventor's Name (typed) David (First) A (Middle Initial) PERCIVAL (Family Name) United Kingdom (Country of Citizenship)

Residence (City) Harwarden (State/Foreign Country) United Kingdom

Post Office Address (Include Zip Code) 4 Overlea Drive, Harwarden, Flintshire, CH5 5HS, United Kingdom

3) INVENTOR'S SIGNATURE: _____ Date _____

Inventor's Name (typed) _____ (First) (Middle Initial) (Family Name) (Country of Citizenship)

Residence (City) _____ (State/Foreign Country)

Post Office Address (Include Zip Code) _____

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